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TOWNSEND and TOWNSEND and CREW LLP

By: Elyse Brownell
Elyse Brownell

PATENT
Attorney Docket No.: 019633-000129US
Neose Ref. No.: NRC00072.1D1C7

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Michael Gilbert *et al.*

Patent No.: 7,462,474

Issued: December 9 2008

Application No.: 10/821,604

Filed: April 4, 2004

For: B1,4-N-ACETYLGALACTOSAMINYL TRANSFERASE POLYPEPTIDES

Customer No.: 20350

Confirmation No. 1518

Examiner: S. Swope

Technology Center/Art Unit: 1652

REQUEST FOR CERTIFICATE OF CORRECTION UNDER 37 CFR § 1.323

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Pursuant to 37 CFR §1.323, Applicants submit herewith a Certificate of Correction (PTO/SB/44) to correct the title of the above-referenced patent. The error was made at the time of filing a Supplemental Response on October 12, 2007, enclosed herewith. As set forth under 37 CFR § 1.20(a), the Examiner is hereby authorized to deduct $100 from Townsend and Townsend and Crew LLP Deposit Account No. 20-1430. This correction does not constitute new matter

Respectfully submitted,

Date: Dec 10, 2008

By: Beth L. Kelly
Reg. No. 51,868

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Attachments
BLK:meb
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UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 7,462,474 B2

APPLICATION NO.: 10/821,604

ISSUE DATE : December 9, 2008

INVENTOR(S) : Michel Gilbert al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Page 1 of patent, paragraph (54), please delete "B1-4,N-ACETYLGLYCOSAMINYL (GALNAC) TRANSFERASE POLYPEPTIDES"

and insert – B1-4,N-ACETYLGALACTOSAMINYL (GALNAC) TRANSFERASE POLYPEPTIDES--

MAILING ADDRESS OF SENDER (Please do not use customer number below):

Beth L. Kelly
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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to:

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

On October 12, 2007

TOWNSEND and TOWNSEND and CREW LLP

By: _____

PATENT
Attorney Docket No.: 019633-000129US
Client Ref. No.: NRC00072.1D1C7

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No. 1518
GILBERT and WAKARCHUK	Examiner: Swope, Sheridan
Application No.: 10/821,604	Technology Center/Art Unit: 1652
Filed: April 8, 2004	SUPPLEMENTAL AMENDMENT
For: LOS LOCUS FROM C. JEJUNI	
Customer No.: 20350	

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Office Action mailed January 27, 2007, and an interview with Examiner Swope on October 11, 2007, please enter the following supplementary amendments and remarks.

Amendments to the Specification begin on page 2 of this paper.

Amendments to the Abstract begin on page 5 of this paper.

Amendments to the Claims are reflected in the listing of claims which begins on page 6 of this paper.

Remarks/Arguments begin on page 7 of this paper.

Amendments to the Specification:

Please replace the title with the following title

β1,4-N-acetylglucosaminyl (GalNAc) transferase polypeptides

Please replace the paragraph beginning at page 1,line 6 with the following amended paragraph:

This application is a continuation application of U.S. Patent Application No. 10/303,128, filed November 21, 2002, now U.S. Patent No. 6,911,337, which is a divisional application of U.S. Patent Application No. 09/816,028, filed March 21, 2001, now U.S. Patent 6,699,705; which is a continuation-in-part of U.S. Application No. 09/495,406, filed January 31, 2000, now U.S. Patent 6,503,744; which claims benefit of US Provisional Application No. 60/118,213, which was filed on February 1, 1999;~~, and is a continuation-in-part of US Application No. 09/495,406 filed January 31, 2000,~~; ~~both of which~~ all four applications are incorporated herein by reference for all purposes.

Please replace the paragraph beginning at page 4, line 10 with the following amended paragraph:

Figures 2A-2B show the genetic organization of the *cst-I* locus from OH4384 and comparison of the LOS biosynthesis loci from OH4384 and NCTC 11168. The distance between the scale marks is 1 kb. Figure 2A shows a schematic representation of the OH4384 *cst-I* locus, based on the nucleotide sequence which is available from GenBank (#AF130466). The partial *prfB* gene is somewhat similar to a peptide chain release factor (GenBank #AE000537) from *Helicobacter pylori*, while the *cysD* gene and the partial *cysN* gene are similar to *E. coli* genes encoding sulfate adenylyltransferase subunits (GenBank #AE000358). Figure 2B shows a schematic representation of the OH4384 LOS biosynthesis locus, which is based on the nucleotide sequence from GenBank (#AF130984). The nucleotide sequence of the OH4382 LOS biosynthesis locus is identical to that of OH4384 except for the *cgtA* gene, which is missing an "A" (see text and GenBank #AF167345). The sequence of the NCTC 11168 LOS biosynthesis locus is available from the Sanger Centre ~~(URL:http//www.sanger.ac.uk/Projects/C_jejuni/)~~ website. Corresponding homologous genes have the same number with a trailing "a" for the

OH4384 genes and a trailing "b" for the NCTC 11168 genes. A gene unique to the OH4384 strain is shown in black and genes unique to NCTC 11168 are shown in grey. The OH4384 ORF's #5a and #10a are found as an in-frame fusion ORF (#5b/10b) in NCTC 11168 and are denoted with an asterisk (*). Proposed functions for each ORF are found in Table 4.

Please replace the paragraph bridging pages 4 and 5 with the following amended paragraph:
Figure 3 shows an alignment of the deduced amino acid sequences for the sialyltransferases. The OH4384 *cst-I* gene (SEQ ID NO:48, first 300 residues), OH4384 *cst-II* gene (SEQ ID NO:3, identical to OH4382 *cst-II*), O:19 (serostrain) *cst-II* gene (SEQ ID NO:9, GenBank #AF167344) , NCTC 11168 *cst-II* gene (SEQ ID NO: 10) and an *H. influenzae* putative ORF (SEQ ID NO:49, GenBank #U32720) were aligned using the ClustalX alignment program (Thompson *et al.* (1997) *Nucleic Acids Res.* **25,** 4876-82). The shading was produced by the program GeneDoc (Nicholas, K. B., and Nicholas, H. B. (1997) ~~URL: http://www.cris.com/~ketchup/genedoc.shtml~~.

Please replace the paragraph beginning at page15, line 11 with the following amended paragraph:
Examples of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul *et al.* (1990) *J. Mol. Biol.* 215: 403-410 and Altschuel *et al.* (1977) *Nucleic Acids Res.* 25: 3389-3402, respectively. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information ~~(http://www.nebi.nlm.nih.gov/)~~. For example, the comparisons can be performed using a BLASTN Version 2.0 algorithm with a wordlength (W) of 11, G=5, E=2, q= -2, and r = 1., and a comparison of both strands. For amino acid sequences, the BLASTP Version 2.0 algorithm can be used, with the default values of wordlength (W) of 3, G=11, E=1, and a BLOSUM62 substitution matrix. (*see* Henikoff & Henikoff, *Proc. Natl. Acad. Sci. USA* 89:10915 (1989)).

Please replace the paragraph beginning at page 49, line 2 with the following amended paragraph:

The primers used to amplify the LPS biosynthesis locus of *C. jejuni* OH4384 were based on preliminary sequences available from the website ~~(URL: http://www.sanger.ac.uk/Projects/C_jejuni/)~~ of the *C. jejuni* sequencing group (Sanger Centre, UK) who sequenced the complete genome of the strain NCTC11168. The primers CJ-42 and CJ-43 (all primers sequences are described in Table 2) were used to amplify an 11.47 kb locus using the Expand™ long template PCR system. The PCR product was purified on a S-300 spin column (Pharmacia Biotech) and completely sequence on both strands using a combination of primer walking and sub-cloning of *Hind*III fragments. Specific ORF's were amplified using the primers described in Table 2 and the Pwo DNA polymerase. The PCR products were digested using the appropriate restriction enzymes (*see* Table 2) and were cloned in pCWori+.

Please replace the paragraph beginning at page 53, line 15 with the following amended paragraph:

Analysis of the preliminary sequence data available at the website of the *C. jejuni* NCTC 11168 sequencing group (Sanger Centre, UK ~~(http://www.sanger.ac.uk/ Projects /C_jejuni/)~~) revealed that the two heptosyltransferases involved in the synthesis of the inner core of the LPS were readily identifiable by sequence homology with other bacterial heptosyltransferases. The region between the two heptosyltransferases spans 13.49 kb in NCTC 11168 and includes at least seven potential glycosyltransferases based on BLAST searches in GenBank. Since no structure is available for the LOS outer core of NCTC 11168, it was impossible to suggest functions for the putative glycosyltransferase genes in that strain.

Please replace the paragraph beginning at page 56, line 1 with the following amended paragraph:

The sequence of the *C. jejuni* NCTC 11168 ORFs can be obtained from the Sanger Centre ~~(URL:http//www.sanger.ac.uk/Projects/C_jejuni/)~~ website.

Amendments to the Abstract:

Please replace the paragraph beginning at page 83, line 7 with the following amended paragraph:

This invention provides prokaryotic ~~glycosyltransferases, including a bifunctional sialyltransferase that has both an α2,3- and an α2,8-activity. A~~ ~~β1,4-GalNAc transferase~~ β1,4-N-acetylglucosaminyl (GalNAc) transferases ~~and a β1,3-galactosyltransferase are also provided by the invention, as are other glycosyltransferases and enzymes~~ involved in synthesis of lipooligosaccharide (LOS). The ~~glycosyltransferases~~ β1,4-GalNAc transferases are obtained from, for example, *Campylobacter* species, including *C. jejuni*. In additional embodiments, the invention provides nucleic acids that encode the ~~glycosyltransferases~~ β1,4-GalNAc transferases, as well as expression vectors and host cells for expressing the ~~glycosyltransferases~~ β1,4-GalNAc transferases.

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1-42. (Cancelled)

43. (Currently amended) An isolated or recombinant β1,4-N-~~acetylgalactosaminyl~~ acetylglucosaminyl (GalNAc) transferase polypeptide;

wherein a nucleotide sequence from a lipooligosaccharide (LOS) locus from *Campylobacter* comprises a polynucleotide sequence that encodes the β1,4-*N*-GalNAc transferase polypeptide and wherein the β1,4-*N*-GalNAc transferase polypeptide transfers a GalNAc residue from a donor substrate to an acceptor substrate; and

wherein the nucleotide sequence from the LOS locus is amplified by PCR from a *Campylobacter* genome using a first primer comprising SEQ ID NO:40 and a second primer comprising SEQ ID NO:41.

44-45. (Cancelled)

46. (Previously presented) The isolated or recombinant β1,4-*N*-GalNAc transferase polypeptide of claim 44, wherein the β1,4-*N*-GalNAc transferase polypeptide further comprises a tag for purification.

47-51. (Cancelled)

REMARKS/ARGUMENTS

With this amendment, claims 43 and 46 are pending. Claims 1-42, 44-45, and 47-51 are cancelled without prejudice. For convenience, the Examiner's rejections are addressed in the order presented in an October 27, 2006, Office Action.

Applicants thank Examiner Swope for her time and assistance in participating in a telephonic interviews with Applicants' representative Beth Kelly on October 11 and 12, 2007. The previously filed response was deemed non-responsive and agreement for proceeding with prosecution was reached.

I. Status of the claims

With this supplemental amendment claim 43 is amended to originally examined language and now recites a β1,4-N-acetylglucosaminyl (GalNAc) transferase polypeptide encoded by a nucleic acid that can be amplified by primers that bind to the 3' and 5' end of the *C. jejuni* LOS locus. Support for β1,4-GalNAc transferase proteins encoded by the *C. jejuni* LOS locus is found throughout the specification, for example, at page 53, line 14 through page 56, line 4. Claim 43 is also amended to recite that the β1,4-GalNAc transferase transfers a GalNAc residue from a donor substrate to an acceptor substrate. Support for β1,4-GalNAc transferase activity is found throughout the specification, for example, at page 20, lines 16-18; page 23, line 12 through page 24, line 16; and page 50, lines 2-14.

II. Priority

According to the Office Action, the priority date of the application is its filing date, April 8, 2004. Applicants have amended the claims to recite a β1,4-N-acetylglucosaminyl (GalNAc) transferase polypeptide encoded by a nucleic acid that can be amplified by primers that bind to the 3' and 5' end of the *C. jejuni* LOS locus. The present application is a continuation application of U.S. Patent Application No. 10/303,128, filed November 21, 2002, which is a divisional application of U.S. Patent Application No. 09/816,028, filed March 21, 2001, which is a continuation-in-part of U.S. Application No. 09/495,406, filed January 31,

2000, which claims the benefit of U.S. Provisional Application No. 60/118,213, which was filed on February 1, 1999. Support for the GalNAc abbreviation, *e.g.*, active β1,4-GalNAc transferase proteins, is found in the priority document, the '213 application at page 35, lines 6-8 and SEQ ID NO:6. Thus, in view of the amendment and the disclosures in the related applications, the priority date of the application should be February 1, 1999.

III. Objections to the title

The Office Action objects to the title of the application because it allegedly is not descriptive of the elected invention. In order to expedite prosecution the title is amended to recite β1,4-N-acetylglucosaminyl (GalNAc) transferase polypeptides. Therefore, withdrawal of the objection to the title is respectfully requested.

IV. Objections to the abstract

The Office Action objects to the abstract because it allegedly is not descriptive of the elected invention. In order to expedite prosecution the abstract is amended to recite β1,4-N-acetylglucosaminyl (GalNAc) transferase. Therefore, withdrawal of the objection to the abstract is respectfully requested.

V. Objections to the specification

The first paragraph of the specification is updated to reflect the current status of all priority documents.

The Office Action objects to the presence of hyperlinks in the specification. In order to expedite prosecution, the specification is amended to remove hyperlinks.

VI. Objections to the claims

Claim 51 is objected to for reciting non-elected subject matter. In order to expedite prosecution, claim 51 is cancelled. Withdrawal of the objection to the claim is, therefore, requested.

VIII. Rejections under 35 U.S.C. §101

Claims 49-51 are rejected for alleged lack of utility because they recite β1,4-N-acetylglucosaminyl transferase activity. Applicants assert that use of the GalNAc abbreviation in claim 43 provides the correct function of the claimed proteins. Support for β1,4-N-acetylgalactosaminyl transferase activity is found in the specification at page 20, lines 16-18; page 23, line 12 through page 24, line 16; and page 50, lines 2-14. Claims 49-51 are cancelled. In view of this amendment, withdrawal of the rejection for alleged lack of utility is respectfully requested.

IX. Rejections for alleged obviousness-type double patenting

Claim 43 is rejected for alleged obviousness-type double patenting over claims 1-3 of US Patent No. 6,210,933 (the '933 patent); claimed 1-7 of US patent No. 6,825,019 (the '019 patent); and claims 1 and 3-5 of US Patent No. 7,078,207 (the '207 patent). To the extent the rejection applies to the amended claims, Applicants respectfully traverse. Claim 43 is amended to recite β1,4-N-acetylgalactosaminyl (GalNAc) transferase polypeptide, rather than glycosyltransferase. The claims of the '933 patent recite α2,3-sialyltransferase activity. The claims of the '019 patent recite β1,3-galactosyltransferase activity. Thus, amended claim 43 is not obvious in view of the '933 and '019 patents.

The '207 patent does recite β1,4-N-GalNAc transferase activity. Applicants stand ready to sign a terminal disclaimer over the '207 patent, in view of the amendment of claim 43.

X. Rejections under 35 U.S.C. §112, second paragraph

Claims 49-51 are rejected for alleged indefiniteness for recitation of "β1,4-N-acetylglucosaminyl (GalNAc) transferase". Claims 49-51 are now cancelled. Claim 43 is amended to recite the originally examined activity "β1,4-N-acetylglucosaminyl (GalNAc) transferase." Applicants expect to complete their answer to this rejection with the next filed response.

XI. Rejections under 35 U.S.C. §112, first paragraph, enablement

Claims 43 and 49-51 are rejected under 35 U.S.C. §112, for allegedly failing to provide enablement for any protein with glycosyltransferase or β1,4-N-GalNAc transferase activity encoded by a nucleic acid that can be generated by PCR using primers of SEQ ID NO:40 and 41 using *Campylobacter* genomic DNA as a template. In order to expedite prosecution, claim 43 is amended to recite a polynucleotide sequence that encodes a β1,4-GalNAc transferase polypeptide. The Office Action also alleges that undue experimentation is required to practice the claimed invention. To the extent the rejection applies to the amended claims, Applicants respectfully traverse the rejection.

Factors such as the amount of guidance presented in the specification and the presence of working examples must be considered to determine whether undue experimentation is required to practice the claimed invention. *See, e.g., Ex Parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int. 1985) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). As described in *Wands*, "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *Wands*, USPQ2d at 1404, quoting *In re Jackson*, 217 USPQ 804 (Bd. Pat. App. & Int. 1982). Moreover, "[a] patent need not teach, and preferably omits, what is well known in the art." MPEP 2164.01 *citing In re Buchner*, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 221 USPQ 481, 489 (Fed. Cir. 1984).

As set forth in the Manual of Patent Examining Procedure (MPEP) § 2164.01, "the test of enablement is not whether any experimentation is necessary, but whether... it is undue." Further, the "fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation" (citations omitted). Finally, claims reading on inoperative embodiments are enabled if the skilled artisan understands how to avoid inoperative embodiments. *See, e.g., In re Cook and Merigold*, 169 USPQ 299, 301 (C.C.P.A. 1971).

According to the Office Action, "the specification teaches the unpredictability of isolating the desired proteins and that the expectation of success is low." Office Action, at page 9. The Office action also alleges that because the size of the LOS locus is different for different *Campylobacter* species "there is little expectation of success in generating the desired nucleic acid molecules using the recited primers." The Office Action also alleges that "the specification states that the function for any putative glycosyltransferase genes in the LOS of Campylobacter jejuni NCTC11163 (sic) is impossible to predict. . ."

In discussing the function of glycosyltransferase genes of the LOS from *C. jejuni* NCTC 11168 as quoted above, the specification is describing the state of the art before the time of filing. This statement does not include the teachings of the specification. The specification provides the first disclosure of a β1,4-N-GalNAc transferase protein encoded by a nucleic acid from the *C. jejuni* LOS locus. Thus, the specification provides the information necessary to allow those of skill to make and use the claimed β1,4-N-GalNAc transferase proteins. The specification provides the amino acid and nucleic acid sequences of five β1,4-N-GalNAc transferase proteins at, *e.g.*, SEQ ID NOs:16-25. β1,4-N-GalNAc transferase assays are disclosed at, *e.g.*, page 20, lines 16-18; page 23, line 12 through page 24, line 16; and page 50, lines 2-14.

The Office Action also alleges that undue experimentation is required by those of skill to make and use the claimed invention. However, the specification demonstrates that those of skill routinely perform large numbers of glycosyltransferase assays. First, the art at the time of filing and the specification provide methods to efficiently assay thousands of proteins for glycosyltransferase activity. These assays can be scaled up even further. For example, the specification discloses a screening strategy used to clone the nucleic acid encoding the CstI protein, a α2,3 sialyltransferase, from *C. jejuni*. Specification at page 47, lines 11-30 and page 52, lines 16-26. The inventors made an expression library of chromosomal DNA from a *C. jejuni* strain and used to transform *E. coli*. They picked 2600 library colonies and combined them into pools of 100 and then assayed each of the 26 library pools. Thus, the initial screening step required only 26 enzymatic assays to screen 2600 library colonies. Out of 2600 library colonies the inventors were able to quickly identify 2 clones with enzymatic activity. Pooled

assay screens of this type are standard and have been used for many years. Thus, using pooled samples, the number of initial assays can be reduced by 100 or 1000 fold. Similar techniques can easily be used by those of skill to identify functional β1,4-GalNAc transferase proteins. Thus, undue experimentation is not required to practice the claimed invention.

In view of the above amendments and arguments, withdrawal of the rejection for alleged lack of enablement is respectfully requested.

XII Rejections under 35 U.S.C. §112, first paragraph, written description

Claims 43 is rejected under 35 U.S.C. §112, for allegedly containing subject matter that was not described in the specification as filed. The Office Action alleges that those of skill would not recognize that the inventors had possession of the claimed genus at the time of filing.

Applicants respectfully traverse the rejection. As currently applied, the specification does comply with US patent law for description of a nucleic acid or amino acid sequence. The Federal Circuit court of Appeals addressed the description adequate to show one of skill that the inventors were in possession of a claimed genus at the time of filing. *See, e.g., Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 63 USPQ2d 1609 (Fed. Cir. 2002). An applicant may also show that an invention is complete by

> . . . disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention . . . *i.e.*, complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. *Id.* at 1613.

Furthermore, "description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces." *See, e.g.*, 66 Fed. Reg. 1099, 1106 (2001).

The specification does provide descriptive support for the full scope of the claimed genus by providing a representative number of species of β1,4-GalNAc transferase amino acid sequences and encoding nucleic acid sequences, *e.g.*, SEQ ID NOs:16-25, and a β1,4-

GalNAc transferase assay used to determine whether polypeptides have the enzymatic activity required by the claims. The assay is described at page 20, lines 16-18; page 23, line 12 through page 24, line 16; and page 50, lines 2-14. This information is more than adequate to meet the written description requirement, particularly in view of *Enzo*, cited above, recent Board decisions, and the interpretation of the Written Description Guidelines evidenced by the USPTO's own Synopsis of Application of Written Description Guidelines.

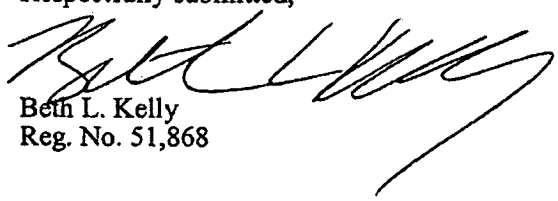
In view of the above arguments and amendments, withdrawal of the rejection for alleged lack of written description is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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Attachments
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